

AMENDMENTS TO THE SPECIFICATION

Kindly amend the paragraph at page 1, line 10 of the specification as follows.

This application is a continuation of and claims priority from United States patent application 09/025,596, filed February 18, 1998 (now U.S.P.N. 6,340,463) (~~now allowed~~), which is a continuation-in-part of U.S. utility application U.S.S.N. 08/911,593, filed August 14, 1997 (now abandoned), which claims benefit from U.S. provisional application U.S.S.N. 60/023,921, filed August 14, 1996 (now abandoned), the entire teachings of which are incorporated herein by reference.

Kindly amend the paragraph at page 2, line 25 of the specification as follows.

The invention also relates to antigenic amino acid subsequences identified by the methods described herein. In particular ~~embodiments~~ embodiments, the invention pertains to an antigenic amino acid subsequence selected from the group consisting of SEQ ID NOS: 1-118.

Kindly amend the paragraph at page 3, line 21 of the specification as follows.

Figure 3 illustrates the predicted antigenic sequences from variable domain 2 (CD2) of various Chlamydia species. The boxed cysteine (C) residue is not part of the native ~~sequence~~ sequence but has been added at the amino terminus for cross-linking to carrier proteins used in immunizations.

Kindly amend the paragraph at page 4, line 12 of the specification as follows.

The identification of antigenic domains described herein is based on the overlap of the most hydrophilic peptide segments of an antigen with those peptide segments with a concomitant predicted peptide flexibility. Increased flexibility allows more conformational degrees of freedom for optimal fit into an antibody binding site. Aromatic amino acids are frequently found in antigenic epitopes although hydrophobic with bulky R groups. This decrease in the relative hydrophobicity and flexibility of ~~th~~ the peptide sequence containing the aromatic residue is compensated for if accessible (i.e., surface of the antigen).

Kindly amend the paragraph at page 8, line 15 of the specification as follows.

As used herein, an “isolated” gene or nucleic acid molecule is intended to mean a gene or nucleic acid molecule which is not flanked by nucleic acid molecules which normally (in nature) flank the gene or nucleic acid molecule (such as in genomic sequences) and/or has been completely or partially purified from other transcribed sequences (as in cDNA or RNA library). For example, an isolated nucleic acid of the invention may be substantially isolated with respect to the complex cellular milieu in which it naturally occurs. In some instances, the isolated material will form party of a composition (for example, a crude extract containing other substances), buffer system or reagent mix. In other ~~circumstance~~ circumstances, the material may be purified to

essential homogeneity, for example as determined by PAGE or column chromatography such as HPLC. Preferably, an isolated nucleic acid comprises at least about 50, 80 or 90 percent (on a molar basis) of all macromolecular species present. Thus, an isolated gene or nucleic acid molecule can include a gene or nucleic acid molecule which is synthesized chemically or by recombinant means. Recombinant DNA contained in a vector are included in the definition of "isolated" as used herein. Also, isolated nucleic acid molecules include recombinant DNA molecules in heterologous host cells, as well as partially or substantially purified DNA molecules in solution. In vivo and in vitro RNA transcripts of the DNA molecules of the present invention are also encompassed by "isolated" nucleic acid molecules. Such isolated nucleic acid molecules are useful in the manufacture of the encoded polypeptide, as probes for isolating homologous sequences (e.g., from other mammalian species), for gene mapping (e.g., by in situ hybridization with chromosomes), or for detecting expression of the gene in tissue (e.g., human tissue which as liver tissue), such as by Northern blot analysis.

Kindly amend the paragraph at page 15, line 9 of the specification as follows.

The invention also relates to immunogenic compositions comprising amino acid sequences described herein, as well as vaccine compositions comprising polypeptides or antibodies described herein. Peptides and antibodies identified by methods described herein can also be used in a variety of assay and protein processing applications,

including, but not limited to, radioimmunoassays, ELISA, antigen capture assays, competitive inhibition assays, affinity chromatography, Western Blotting, Labeled-antibody assays such as immunofluorescence assays, immunohistochemical staining assays and immunoprecipitation assays. The ~~antibodies~~ antibodies, alone or linked to particular toxins, can also be used for a variety of therapeutic and other purposes, including removing specific lymphocyte subsets, inhibiting cell function, inhibiting graft rejection, alleviating or suppressing autoimmune disease, and attaching to tumors.

Kindly amend the paragraph at page 17, line 17 of the specification as follows.

The individual vertebrate is inoculated with the nucleic acid vaccine (i.e., the nucleic acid vaccine is administered), using standard methods. The vertebrate can be inoculated subcutaneously, intravenously, intraperitoneally, intradermally, intramuscularly, topically, orally, rectally, nasally, buccally, vaginally, by inhalation spray, or via an implanted reservoir in dosage formulations containing conventional non-toxic, physiologically acceptable carriers or vaccines. Alternatively, in a preferred embodiment, the vertebrate is ~~inoculated~~ inoculated with the nucleic acid vaccine through the use of a particle acceleration instrument (a “gene gun”). This form in which it is administered (e.g., capsule, tablet, solution, emulsion) will depend in part on the route by which it is administered. For example, for mucosal administration, nose drops, inhalants or suppositories can be used.

Kindly amend the paragraph at page 19, line 6 of the specification as follows.

The teachings of all references cited herein are ~~specifically~~ specifically incorporated herein by reference. The teachings of Attorney Docket No. VDB96-02pA2, entitled “Diagnosis and Management of Infection Caused by Chlamydia” by William M. Mitchell and Charles W. Stratton, filed concurrently with the present application, are also incorporated herein by reference in their attorney.

Kindly amend the paragraph at page 22, line 21 of the specification as follows.

2) Antigenicity of 76k D protein of *C. pneumoniae*:

C. pneumoniae expresses a gene encoding a unique 76 kD protein (Perez-Melgosa et al., Infect. Immun. 62:880-0886 (1994)). Hydrophilicity/peptide flexibility analysis predicts the sequence of amino acids 302-315 (KPKESKTDSVERWS; SEQ ID NO: 1) to be highly antigenic; the peptide has been extended towards the carboxyl terminus to include aromatic and additional hydrophilic amino acid residues. The predicted sequence has been further modified to include an adjacent relatively hydrophilic region containing an aromatic amino acid (tryptophan). Other potential antigenic peptides based on either hydrophilicity or peptide flexibility and extended to include ~~emino~~ amino acids found in hydrophilic or flexible segments, as well as inclusion of aromatic amino acids immediately adjacent to the predicted antigens, are illustrated in Table 3.

Kindly amend the paragraph at page 24, line 1 of the specification as follows.

a) ~~C. pneumonia~~ pneumoniae DNAK/heatshock protein 70:

Hydrophilicity/peptide flexibility analysis predicts a highly antigenic sequence in the C-terminal region of the expressed protein. This antigenic domain and its homologous human protein are illustrated in Table 4; vertical lines indicate residue homology while “+” signs indicate retention of a positive charge at the site. Amino acid residues 522-529 are either homologous to the human protein or possess preservation of charge (i.e., AA 525-529). Antibodies against this epitope would be expected to possess cross-reactivity with the human 70 kD heat shock protein. Peptides incorporating the C-terminal end of this common region with the non-homologous sequence would be expected to identify Chlamydial-specific antibodies. Two embodiments of this invention include the full length peptide (AA 521-536) and the Chlamydial-specific epitopic sequence identified as AA 527-536 or truncated for the identification of Chlamydia-specific antibodies. Table 5 illustrates other potential antigenic sequences for the DNAK protein expressed by *C. pneumoniae* based on either peptide flexibility or hydrophilicity and extended to include amino acids found in adjacent hydrophilic or flexible segments, as well as inclusion of aromatic amino acids immediately adjacent to the predicted antigens.